

### **Detailed Action *Election/Restrictions***

Applicant's response to the Requirement for Restriction, filed on July 22, 2009 is acknowledged.

Applicant has elected the invention of Group I, Claims 2-5 and 11-17, drawn to a method for identifying a compound which modulates an interaction between a first and a second polypeptide, the method comprising contacting *in vitro* a non-transgenic cell having a first polypeptide comprising a binding portion of a KRC polypeptide and a second polypeptide comprising a binding portion of a polypeptide selected from the group consisting of GATA3, SMAD or Runx2, classified in class 435, subclass 4.

Within Group I, Applicant has elected the following species, wherein:

- i) Claims 1 and 22 are generic to the host cell is a mouse T cell;
- ii) determination method steps from the lists recited in claims 9-11 and 13-15, is co-immunoprecipitation (Claim 11);
- iii) second polypeptide indicator recited in Claims 1, 4-5 and 22 is GATA3; and
- iv) biological activity species that is to be measured from the list recited in Claims 13, 19 and 21 is Th2 cell differentiation.

### ***Amendments***

In the reply filed December 22, 2011, Applicant has cancelled Claims 1-67 and 70, and withdrawn Claims 69, 72, 74-77 and 79, and amended Claim 68.

Claims 69 and 77 are drawn to non-elected determination method step species, per the recitation of a reporter gene which is an art-recognized heterologous nucleic acid construct (pg 30, lines 8-10, 22-26).

Claims 72 and 74-76 are drawn to non-elected transgenic host cells that properly belong to Group II.

Claim 79 recites a cDNA molecule (SEQ ID NO: 1), and thus is a transgenic nucleic acid molecule that properly belongs to non-elected Group II.

Claims 69, 72, 74-77 and 79 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

This application contains claims drawn to an invention nonelected with traverse in the reply filed on July 22, 2009. Applicant is reminded that the restriction/election requirement was made final in the Office Action of October 7, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP §821.01.

Claims 68, 71, 73, 78 and 80-81 are under consideration.

If the claims are amended, added and/or canceled in response to this Office Action, then Applicant is required to follow Amendment Practice under 37 C.F.R. §1.121 AND A CLEAN COPY OF ALL PENDING CLAIMS IS REQUESTED.

### ***Priority***

This application is a 371 of PCT/US04/36641 filed November 3, 2004, which is a continuation of U.S. application 10/701,401 filed November 3, 2003, which is a continuation-in-part of PCT/US02/14166 filed May 3, 2002. Applicant's claim for the benefit of a prior-filed application parent provisional application 60/288,369 filed May 3, 2001 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

### ***Examiner's Note***

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the December 22, 2011 response will be addressed to the extent that they apply to current rejection(s).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Information Disclosure Statement***

Applicant has filed Information Disclosure Statements on December 22, 2011 that has been considered.

The signed and initialed PTO Forms 1449 are mailed with this action.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. **Claims 68, 71, 73, 78 and 80-81 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Emerson (U.S. 2002/0022021; of record) in view of Haenlin et al (1997; of record), Matthews et al (2000; of record), Cubbada et al (1997; of record), (1995; of record in IDS), Wu et al (1996; of record in IDS), Hicar et al (2001; of record in IDS) and Ting et al (1996; of record), as applied to Claims 68, 71, 73, 78 and 80 above, and in further view of Lee et al (1998; of record) and Wu et al (Nucleic Acid Res. 21(22):5067-5073, 1993).

With respect to the newly recited limitation of "selecting a compound", Emerson discloses the screening method is to identify small molecules. While Emerson does not disclose *ipsis verbis* the step of 'selecting', one of ordinary skill in the art would immediately understand

that upon identifying an agent having the desired properties, it is axiomatic that one would 'select' said agent because "[I]n this way, drugs are developed..." [0017]. To put it another way, it is illogical to not select an agent that has been identified for having the desired properties.

***Response to Arguments***

Applicant argues that the cited art fails to provide the motivation to develop such a screening method.

Applicant's argument(s) has been fully considered, but is not persuasive. Emerson discloses that one would be motivated to screen compounds for specific proteins to identify high target specificity, drastically reducing the undesirable side effects of drugs that grossly inhibit gene activation in general [0041]. Lee et al taught that one would be motivated to find important targets for the treatment of IL-5-associated allergic diseases, for which IL-5 is an important regulator and that IL-5 expression is restricted to Th2 cells, and also alternative approaches to therapy (pg 2343; pg 2352).

It would have been obvious to one of ordinary skill in the art to modify the method of identifying a compound which modulates an interaction between a mammalian KRC polypeptide and a mammalian GATA-3 polypeptide to further comprise the step of determining the ability of the compound to modulate Th2 cell differentiation with a reasonable expectation of success because those of ordinary skill in the art had long recognized that KRC may be involved in T cell development and GATA-3 is involved specifically in Th2 cell development.

Applicant argues that there was no reasonable expectation of success that such a screening method would be successful. It could not have been predicted that a Shn CCHC zinc finger would bind to the Drosophila GATA-I homologue, let alone whether KRC would bind to GATA-3, let alone that one could identify a compound of interest that downmodulates Th2 cell differentiation by selecting from the library of test compounds a compound that downmodulates the ability of the mammalian KRC polypeptide and the mammalian GATA3 polypeptide to interact as compared to an appropriate control; and further comprising testing the ability of that compound to downmodulate Th2 cell differentiation as presently claimed.

Applicant's argument(s) has been fully considered, but is not persuasive.

As a first matter, Matthews et al taught that the topology of CCHC zinc-fingers, present in Ush, is essential for GATA-binding, thereby establishing for one of ordinary skill in the art a reasonable prediction that Shn, an art-recognized CCHC zinc-finger and KRC-like protein, may also bind to a GATA protein via the CCHC zinc-finger.

As a second matter, Wu et al taught the cloning of KRC from murine thymocytes. Ting et al taught that GATA-3 is expressed in thymocytes and T cells, and is required for T cell development, both KRC and GATA-3 are expressed in the same cells, Th2, and are both involved in the differentiation of said cells, thereby establishing for one of ordinary skill in the art a reasonable prediction that KRC may bind GATA-3 because both proteins are expressed in the same cells (Wu et al, Hicar et al, Ting et al)

As a third matter, Cubbada et al teach that cell differentiation [increased or decreased bristle cell differentiation] is sensitive to the downmodulated interaction between GATA (Pnr) protein and its CCHC zinc-finger partner protein (Ush) (pg 3085, Figure 1; pg 3086, Figure 2; pg 3087, Figure 3). Thus, one of ordinary skill in the art would have a reasonable expectation of success that upon testing a compound having the ability to disrupt an interaction between KRC and GATA-3, one may identify a compound which downmodulates Th2 cell differentiation.

The person of ordinary skill in the art is a hypothetical person who is presumed to have known the relevant art at the time of the invention. Factors that may be considered in determining the level of ordinary skill in the art may include: (1) "type of problems encountered in the art;" (2) "prior art solutions to those problems;" (3) "rapidity with which innovations are made;" (4) "sophistication of the technology; and" (5) "educational level of active workers in the field. In a given case, every factor may not be present, and one or more factors may predominate." *In re GPAC*, 57 F.3d 1573, 1579, 35 USPQ2d 1116, 1121 (Fed. Cir. 1995); *Custom Accessories, Inc. v. Jeffrey-Allan Industries, Inc.*, 807 F.2d 955, 962, 1 USPQ2d 1196, 1201 (Fed. Cir. 1986); *Environmental Designs, Ltd. V. Union Oil Co.*, 713 F.2d 693, 696, 218 USPQ 865, 868 (Fed. Cir. 1983).

The combination of prior art cited above satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc.* (KSR), 550 U.S., 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness

include: (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art.

It would have been obvious to one of ordinary skill in the art to assay a first polypeptide comprising a KRC polypeptide and a second polypeptide comprising a GATA3 polypeptide in a method for identifying a compound which modulates an interaction between a first polypeptide and a second polypeptide because the design incentives provided a reason to make such an adaptation, the invention resulted from application of the prior knowledge in a predictable manner, and "a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipate success, it is likely that product not of innovation but of ordinary skill and common sense." In the instant case, a) the prior art within the same field of endeavor as that of Applicant's invention taught a similar or analogous method to assay a first polypeptide and a second polypeptide comprising a GATA polypeptide in a method for identifying a compound which modulates an interaction between a first polypeptide and a second polypeptide (Emerson), b) there were design incentives which would have prompted adaptation of the known method, specifically the recognition of a protein-protein interaction between a GATA factor and a polypeptide comprising a CCHC motif, such as KRC (Haenlin et al, Matthews et al, Cubbada et al, Wu et al, Hicar et al), c) the differences between the claimed invention and the prior art were encompassed in known variations or in a principle known in the prior art, specifically the routinely practiced assaying of physical interactions between a first polypeptide of interest and second polypeptide of interest by those of ordinary skill in the art pursuing known options within his or her technical grasp (Emerson, Haenlin et al), d) those of ordinary skill in the art in view of the design incentives could have implemented the claimed variation of the prior art, and the claimed variation would have been predictable, specifically in light of the topology of CCHC zinc-fingers, present in KRC and essential for GATA-binding (Matthews et al, Cubbada et al, Hicar et al), and e) GATA-3 was recognized in the prior art to be expressed in the same cell type as KRC, specifically T cells and T lymphocytes (Wu et al, Hicar et al, Ting et al).

The cited prior art meets the criteria set forth in both *Graham* and *KSR*, and the teachings of the cited prior art provide the requisite teachings and motivations with a clear, reasonable

expectation of success. Thus, absent evidence to the contrary, the invention as a whole is *prima facie* obvious.

### ***Conclusion***

2. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/  
Examiner, Art Unit 1633

Application/Control Number: 10/578,402  
Art Unit: 1633

Page 8